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Advantages of Ultrafast™ ultrasound in the screening for renal artery disease

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Abstract

Aim: Renal artery disease is the most common cause of secondary hypertension worldwide. B-mode and Doppler ultrasound are considered the modalities of choice for the imaging of the renal arteries. However, an adequate examination can be plagued by difficulties in patients with unfavorable anatomy. UltraFast™ ultrasound is faster, performed with higher frame rates, and enables prospective and retrospective data analysis with quantification of flow data in the obtained image, so it may be able to resolve some of the difficulties encountered during conventional ultrasound examinations in patients with suspected renal artery disease. **Material and methods:** Comparison of the duration of conventional and UltraFast™ Doppler examinations of segmental renal arteries was performed on 52 young, healthy volunteers. Duration times were summarized using the median and interquartile range, and comparisons between the two methods were performed using the Wilcoxon test for paired samples. **Results:** The duration of UltraFast™ ultrasound examinations was significantly shorter in comparison to conventional ultrasound for both kidneys and in total ($p < 0.001$, median difference in duration 65 s, median 64% shorter duration of analysis), while both conventional and UltraFast™ ultrasound examinations demonstrated consistent velocity measurements with very high correlation ($Rho = 0.94$, $p < 0.001$). **Conclusions:** The study provides evidence that UltraFast™ ultrasound is faster than conventional Doppler ultrasonography for the assessment of renal artery disease in healthy adults without a history of renal disease. The findings have important implications for clinical practice, as they suggest that UltraFast™ imaging could offer a more efficient and time-saving approach to vascular imaging in patients with suspected renal artery disease.

Introduction

Renal artery disease (RAD), also called renal artery stenosis (RAS), is diagnosed when the narrowing of the lumen of the renal artery is $\geq 60\%$. RAD is the most common cause of secondary hypertension worldwide, affecting up to 35% of patients with secondary hypertension. RAD is most typically caused by atherosclerosis, which accounts for about 90% of the cases, while fibromuscular dysplasia (FMD), extrinsic compression syndromes and vasculitides account for most of the remaining cases, with FMD being the most common cause in younger patients (especially women). It usually involves the ostial portion of the renal artery, and the patients often have associated coronary, carotid and peripheral artery disease. It is more

commonly associated with the male gender, hypertension, smoking, diabetes mellitus, chronic kidney disease, and aortoiliac occlusive disease⁽¹⁻⁴⁾. The prevalence of RAD increases with age, and it is present in 5–10% of the general population, with a higher prevalence in high-risk populations whose characteristics have been listed previously. In about 20% of patients, the disease is present bilaterally⁽⁵⁾.

RAD is a progressive disease in nature, and the risk of progression is highest in patients with high-grade stenosis, severe hypertension, and diabetes. Less than 10% of patients with RAS progress to high-grade stenosis or occlusion within five years, and deterioration of renal function is rare with unilateral RAS, but more common with bilateral RAS or with a single functioning kidney⁽⁶⁾.

Renal arteriography is considered the golden imaging standard for the diagnosis of RAD. However, it is not the first-line imaging modality, and less invasive modalities, such as Doppler ultrasound (DUS), are currently employed for this purpose.

DUS is a noninvasive, relatively inexpensive technique and the first-line imaging modality to screen for RAS. It can be repeated to assess the progression of stenosis and its hemodynamic consequences (e.g. flow velocity and vascular resistance), however, it has a tendency to overestimate the degree of stenosis^(7,8). Peak systolic velocity (PSV) in the main renal artery has shown the best sensitivity (85%) and specificity (92%) to identify significant stenosis angiographically⁽⁹⁾. Therefore, criteria other than PSV should be used to support the diagnosis, such as renal resistive index (RRI), which may help to identify more severe RAS and provide additional information on patient response to intervention^(3,8). In duplex ultrasound, the peak systolic and end-diastolic velocities of the renal artery as well as the ratio of velocities in the renal artery to the aorta are obtained. The RRI is then determined by subtracting the end diastolic velocity from the peak systolic velocity, with normal values ranging from 0.50 to 0.70, which can be abnormal both when high and low^(10,11). The RRI can also be changed by both renal and extrarenal factors. Because of that, a low RRI can reflect a RAS above 70% or valvular aortic stenosis, thoracic or suprarenal abdominal aortic stenosis, tachycardia, hypervolemia, and parasympathetic activation, which are all extrarenal factors. In contrast to that, a higher RRI can reflect vasoconstriction, arteriolosclerosis, increased interstitial and increased venous pressure as intrarenal influences or adrenergic hyperactivity, bradycardia, and increased systemic pulse pressure as extrarenal determinants⁽¹²⁾. In cases of significant RAS, the obtained DUS post-stenotic flow wave is characterized by a typical parvus-tardus pattern and the RRI is lowered. This lowered RRI then suggests that the ischemic kidney is sheltered from damage by vasodilation caused by the self-regulated intrarenal mechanism. However, if RAS persists, chronic renal disease leads to an increase in the values of the RRI due to an increase in the parenchymal vascular renal resistance, which may mask the diagnosis and hemodynamic effects of RAS. A low RRI may predict renal function recovery in the case of a successful revascularization of the renal artery, while an increased RRI is not associated with recovery of the renal function after revascularization⁽¹³⁾. An adequate renal DUS examination requires an experienced operator, and may be difficult to perform in overweight subjects, patients who have recently had food intake, or have a lot of bowel gas and may miss accessory renal arteries⁽⁷⁾.

Computed tomography angiography (CTA) and magnetic resonance angiography (MRA) are recommended imaging modalities for the confirmation of RAD after DUS was performed. They both show equally high sensitivities and specificities for the detection of RAD and also provide additional anatomical information and can be used to guide intervention, if necessary. Digital subtraction angiography (DSA) still remains the golden standard for the diagnosis of RAD. A major advantage of DSA over other imaging methods is the possibility to measure the pressure gradient across the lesion, which is especially useful for moderate stenosis. However, because of the risks associated with the invasive nature of DSA imaging, DSA is usually used to visualize and quantify the stenosis before endovascular intervention^(14,15).

UltraFast™ (SuperSonic® MACH™ 30, Hologic, Marlborough, USA) imaging is a newly developed modality of medical ultrasonogra-

phy which, depending on the application, provides more than 100 times higher frame rates than conventional ultrasound scanners and scanning of the whole region of interest in a single insonification. Conventional ultrasound imaging is performed step by step by sequential insonification of the medium using focused beams. Each of those focused beams then allows reconstruction of only one image line. In that way, the frame rate is determined by the time necessary to transmit the beam, receive it, and process it to form an image. Therefore, as soon as higher frames are required, the limitations of conventional ultrasound imaging become apparent, since conventional ultrasound systems are built on a serialized architecture and the images are processed in a step-by-step fashion from several equivalent transmits. UltraFast™ ultrasound overcomes this obstacle by computing as many planes as possible in parallel. This enables UltraFast™ ultrasound systems to compute a full image from a single transmit, regardless of image size and its other characteristics. By using a parallel architecture, the frame rate is limited only by the time the ultrasound pulse needs to propagate in the medium and return to the transducer, and it is no longer limited by the number of reconstructed lines^(16,17). There are several ways to construct an ultrafast imaging architecture. The one used in UltraFast™ ultrasound is based on the use of plane wave insonifications. A plane wave is created by using flat delays on the transmit elements of the ultrasound probe, enabling insonification of the whole area of interest. The echoes that are sent back are then registered and processed by the scanner, creating an image of the examined area. However, plane wave imaging removes the transmit focalization step, reducing the contrast and resolution of the obtained image. This is resolved by sending several tilted plane waves into the medium, which are then coherently summated to form a full image^(18,19).

The idea of ultrafast ultrasound was first introduced more than 40 years ago, but was limited by the processing technology at the time. To achieve ultrafast imaging, image processing must be performed on a parallelized, typically software-based, platform, which could not be achieved before the onset of new powerful processing units in the 2000s. Thanks to these advancements in the processing power of personal and commercial computers over the last decades, it recently been implemented more and more often in commercial ultrasound diagnostic devices⁽²⁰⁾. It has resolved the low frame rate limitation of conventional ultrasound devices by significantly reducing the number of insonifications required to generate an equivalent image. This technology has allowed for the development of a number of new ultrasound imaging modalities, such as Ultrafast Doppler and Ultrafast Pulse Wave Velocity (uffPWV)⁽²¹⁾.

In a conventional Doppler ultrasound device, vascular imaging is performed by two modes in addition to B-mode ultrasound: color flow imaging (CFI) and pulsed-wave Doppler (PW Doppler)⁽²²⁾. Quantitative analysis during an examination using conventional Doppler ultrasound is only possible by limiting the region of interest (ROI) to a single acoustic line. During the examination, the operator constantly has to switch between the CFI and PW Doppler modes, and analyze using PW the regions of interest pointed out by the CFI mode. An upgrade on the method, called the triple mode, which includes simultaneous CFI and PW Doppler imaging, has been developed to speed up the workflow. However, it also has its drawbacks, such as reduced frame rates and a need for additional processing power. This can result in a time lag of the acquired Doppler signals at the sides of the image⁽²³⁾. In contrast to conventional ultrasound, UltraFast™ enables merging of CFI and

PW Doppler mode in a single acquisition with quantitative data assessment in all pixels simultaneously. Since it relies on plane waves and not focused beams during image acquisition, there is no time lag at the sides of the image. Several tilted plane waves are sent into the medium, and the received backscattered echoes are then used to reconstruct images, as mentioned earlier. When performing UltraFast™ ultrasound examinations, a single-shot acquisition mode is initiated from the conventional color Doppler imaging mode superimposed on B-mode ultrasound. UltraFast™ ultrasound acquisition is then initiated, which usually lasts 2 to 4 seconds. The image is frozen, and the operator can then assess the obtained data, choose the single or multiple best frames for analysis, and even perform a retrospective spectral analysis of the color box, if necessary. In addition to that, using UltraFast™, a short clip of multiple regions of interest can be obtained, providing a more precise comparison of both mean and peak flow velocities originating from the same cardiac cycle⁽²⁴⁾.

The aim of this study was to compare the efficiency of UltraFast™ ultrasound and conventional Doppler in the screening for renal artery disease in healthy volunteers, which may have important implications for clinical practice.

Materials and methods

This prospective single-center study conducted at our institution aimed to investigate the presence of renal artery disease in 52 healthy volunteer adults between the ages of 25 and 58 years (median age: 30 years), without a history of renal disease. All patients were examined with the same ultrasound scanner (SuperSonic® MACH™ 30, Hologic, Marlborough, USA, product version 6.2.0, software 6.2.23751) using a 1–6 MHz frequency 79 mm long curved probe, by an experienced radiologist with over five years of practice in abdominal and vascular ultrasound. B-mode ultrasound, conventional Doppler for CFI and PW Doppler were performed in the same session as well as UltraFast™ ultrasound.

The patients were examined in a supine or lateral decubitus position if needed to facilitate kidney visualization. Sagittal view of each kidney was obtained in B-mode using an Abdominal – Renal preset to locate the hilum and blood vessels. Next, imaging parameters such as depth, focal zone, and time-gain compensation were optimized. The aforementioned steps were considered the standard procedure preceding both conventional and UltraFast™ ultrasound to ensure that the time required for these actions would be the same for both techniques. Individual topographic anatomy was regarded as the only factor having a significant effect on the time required for B-mode visualization and hence was not recognized as significant in comparison of conventional vs UltraFast™ ultrasound imaging. The conventional color Doppler ultrasound mode was then applied, the targeted renal vessels being segmental renal arteries, one in the upper pole of the kidney, one in the interpolar part, and one in the lower pole of the kidney. Gain was optimized as maximal without background noise present. Lowest pulse-repetition frequency without aliasing artefact was adjusted. PW Doppler was then performed with real-time adjustments of sample volume and Doppler angle. The waveforms were obtained for at least three consecutive heartbeats. Time needed to perform all the steps from the start of CDFI to obtaining spectral waveforms was recorded. Next, UltraFast™ Doppler acquisition was done on conventional CDFI with mechanically

preset duration. The UltraFast™ clip was then reviewed, and the optimal frame was selected for flow analysis. In the next step, spectral analysis was added with adjustment of sample volumes and Doppler angles. Time required for all steps from CDFI image to obtaining waveforms using UltraFast™ acquisition was recorded. PSV and end diastolic velocities (EDV) were recorded for each vessel examined using both methods. However, time required for the measurement of flow velocities on waveforms obtained via both conventional PW and Ultrafast™ imaging was considered insignificant due to the same process required for caliper positioning in both methods and was excluded from analysis. An example of images obtained for conventional and Ultrafast™ Doppler imaging is given in Fig. 1. The study

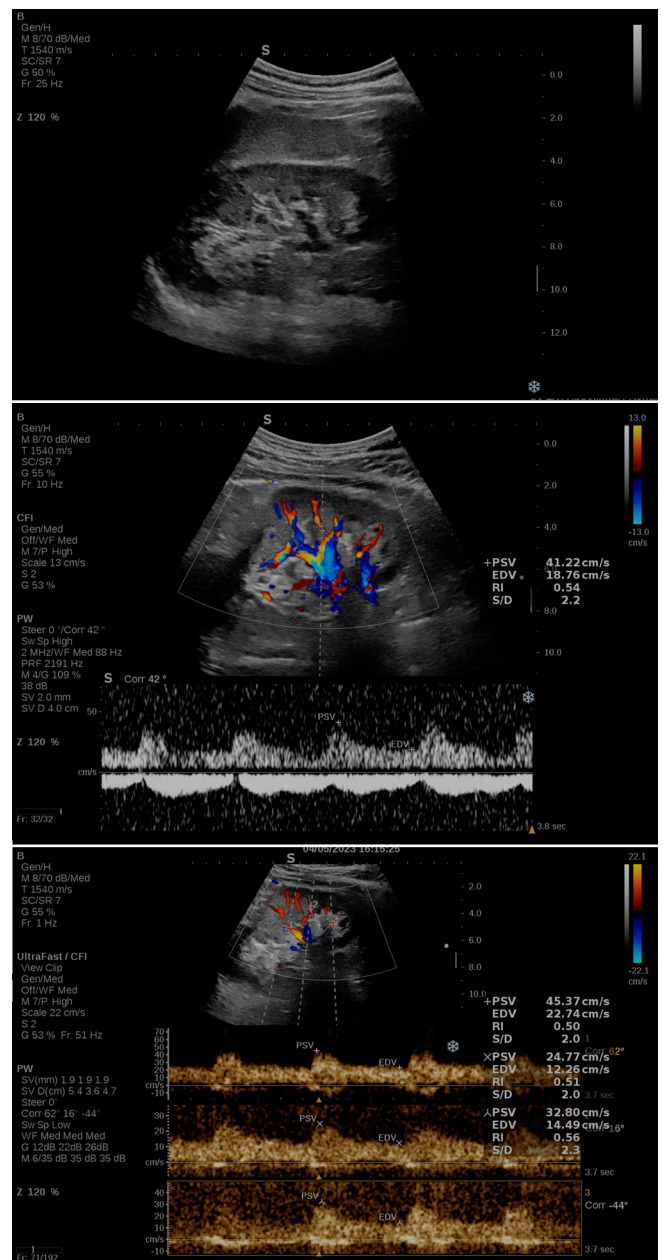


Fig. 1. The kidneys were first visualized using B-mode ultrasound (upper image). Conventional color Doppler imaging was then performed with pulse-wave spectral analysis (middle image). Next, UltraFast™ acquisition was performed with spectral analysis of segmental arteries (lower image)

was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the University Hospital Dubrava in Zagreb, Croatia. Written informed consent was obtained from the patients included in the study.

Normality of distribution of numerical variables was tested using the Shapiro-Wilks test. Due to non-normal distribution, numerical variables were summarized using the median and interquartile range (IQR). Comparisons between UltraFast™ ultrasound and conventional Doppler in the same patients were performed using the Wilcoxon test for paired samples. Percentage improvement in the duration of analysis was obtained by dividing UltraFast™ with conventional time of analysis and was taken as a measure of efficacy. Efficacy was compared between the sex and age subgroups using the Mann-Whitney U test. Correlations between the obtained measurements and conventional and ultrafast methods were analyzed using the Spearman rank correlation and quantified with Spearman's Rho coefficient of correlation. *P* values <0.05 were considered statistically significant. All analyses were performed using the MedCalc statistical software version 20.114 (MedCalc Software Ltd, Ostend, Belgium).

Results

We analyzed a total of 52 patients who underwent examinations with both methods. The median age was 30 years, IQR (28–32). There were 27 (51.9%) female and 25 (48.1%) male patients. The durations of the conventional and UltraFast™ ultrasound examinations for the right kidney, left kidney, and in total are shown in Fig. 2.

Median conventional ultrasound examination times were 53.5 s IQR (44–69.5) for the right kidney, 43.5 s IQR (37–60.5) for the left kidney, and 101.5 s IQR (87.5–119.5) for the total duration of the examination. Conventional ultrasound required significantly longer examination times for the right kidney in comparison to the left kidney (median 53.5 s vs 43.5 s, respectively, *p* = 0.009). Median UltraFast™ ultrasound times were 18 s IQR (15–21) for the right kidney, 16.5 s IQR (13–21.5) for the left kidney, and 36 s IQR (32–41.5) for the total duration of the examination. No significant difference was observed for the duration of the right and left kidney analysis (*p* = 0.186). UltraFast™ ultrasound lengths of examination were significantly shorter in comparison to conventional ones for the right kidney (*p* <0.001, median difference in duration 35.5 s, median 67% shorter duration of analysis), left kidney (*p* <0.001, median difference in duration 27 s, median 65% shorter duration of analysis), and in total (*p* <0.001, median difference in duration 65 s, median 64% shorter duration of analysis). Differences between the conventional and UltraFast™ ultrasound examination lengths per patient are depicted in Fig. 3 A for the right kidney, Fig. 3 B for the left kidney, and Fig. 3 C for the total duration of the examination, respectively. No significant differences in the efficacy of UltraFast™ ultrasound vs conventional ultrasound examinations were present regarding age and sex (*p* <0.05 for all analyses). Ten study patients underwent Ultrafast assessment because the conventional Doppler examination was unsuccessful, however, they were not included in the study results because their data was incomplete due to the unsuccessful conventional Doppler examination.

We further compared the obtained peak systolic velocity measurements with both methods in a subset of patients. Both conventional

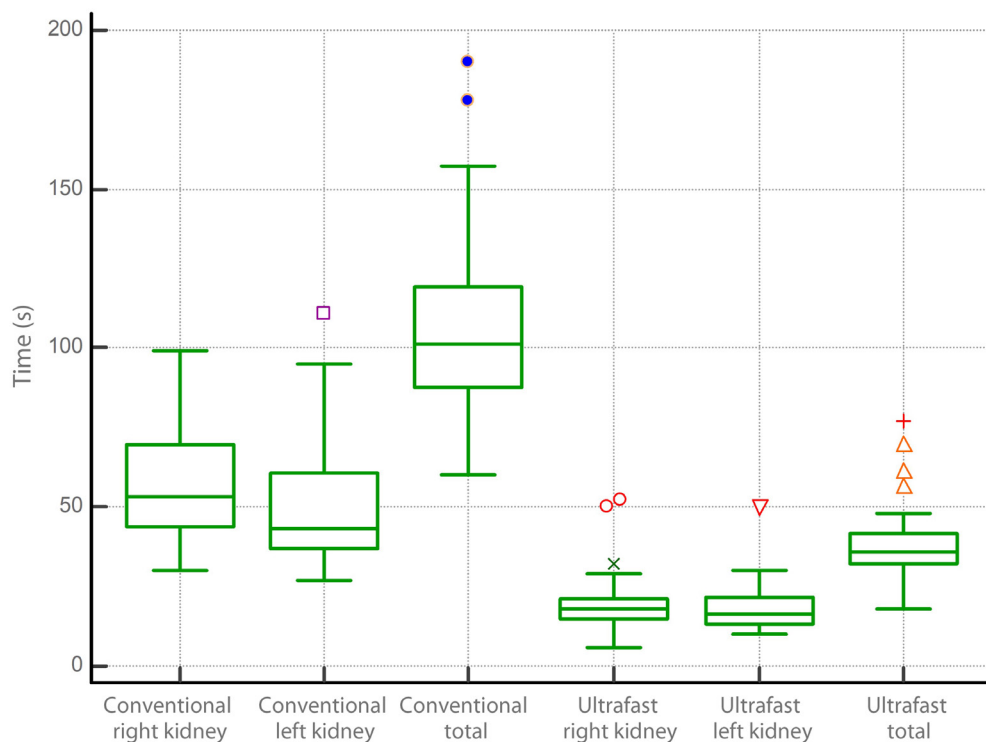


Fig. 2. The duration in seconds of ultrasound examinations for the right kidney, left kidney, and in total are shown separately for conventional and UltraFast™ ultrasound

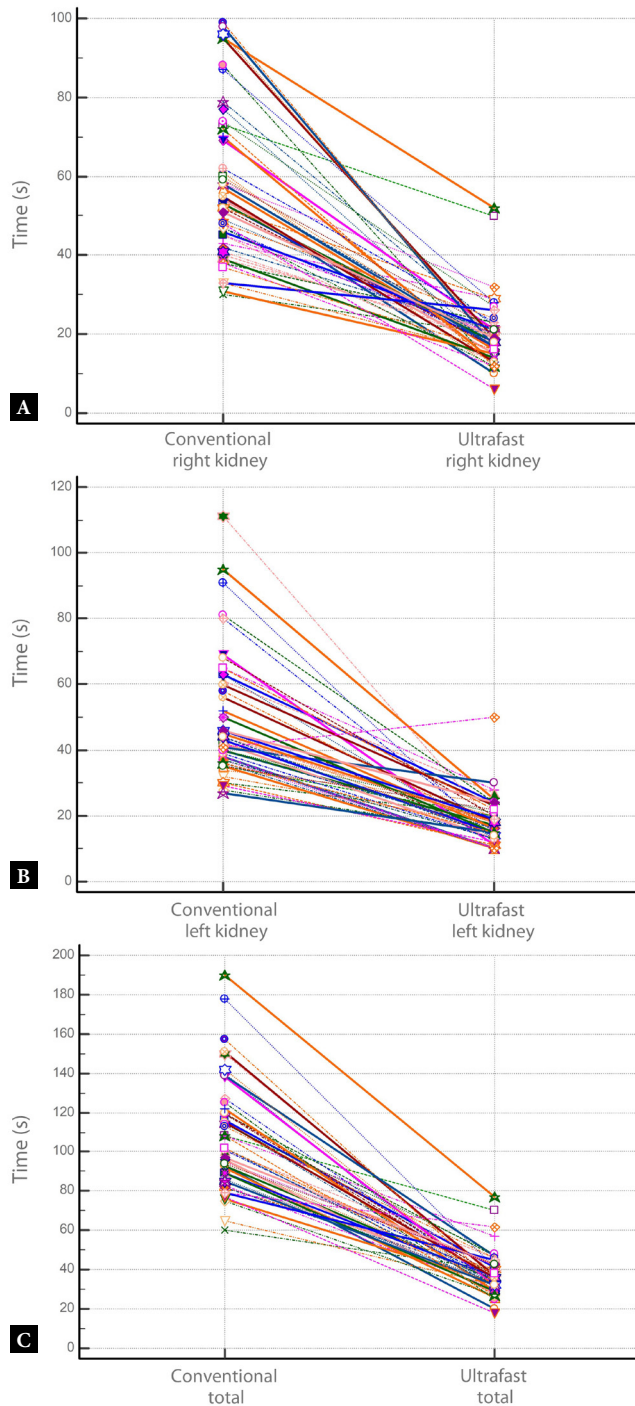


Fig. 3. Differences in seconds between conventional and UltraFast™ times per patient for **A.** right kidney, **B.** left kidney, and for **C.** total time of analysis

and UltraFast™ ultrasound demonstrated consistent measurements and very high correlation ($Rho = 0.94, p < 0.001$).

Discussion

DUS is a non-invasive, safe, painless, and relatively inexpensive technique, and the first-line imaging modality in the screening for

RAD⁽⁷⁾. However, it requires an experienced operator and patient collaboration during the examination. During the procedure, the patient should be able to achieve multiple breath-holds for an adequate amount of time, during which the operator has to visualize the kidney and the renal arteries in the cranial, middle and caudal thirds of the kidney. Consequently, there is often a small but significant interobserver variability in the measured values of the velocities and renal resistive indices across different operators⁽²⁵⁾. UltraFast™ is a new ultrasound technique that uses plane wave ultrasound waves to quickly measure blood flow in multiple directions. It is considered fast and more accurate than conventional Doppler ultrasound, which uses a single narrow beam to measure blood flow in one direction at a time. During examinations, in contrast to conventional techniques, patients are required to achieve only one breath-hold, during which the imaging software analyses and records a short clip to allow post-procedural interpretation⁽²⁴⁾.

In this single-center study, the median conventional ultrasound examination times for both the right and left kidneys and the total duration of the examination were significantly longer for conventional ultrasound in comparison to UltraFast™ ultrasound. There were no significant differences in the efficacy of UltraFast™ ultrasound in comparison with conventional ultrasound examinations regarding patient age and sex. Our study has shown UltraFast™ ultrasound to be faster than conventional Doppler ultrasonography, while both conventional and ultrasound methods have demonstrated consistent measurements of flow velocities. This increased speed allows for more precise and accurate measurements of blood flow in real-time with better spatial resolution and less motion artefacts. Additionally, the increased speed of imaging enables more efficient data collection, reducing the time needed for a complete examination. Since the collected data can also be retrospectively analyzed, this may provide benefits when additional evaluation is required, for example in patients with subsequently diagnosed renal masses. In comparison to conventional ultrasound, UltraFast™ may also have benefits when examining patients with irregular cardiac rhythm, which often impedes conventional ultrasound analysis.

The study has its limitations. Only healthy volunteers that were able to collaborate during the examination were included in the study, whereas the majority of patients with suspected RAD are of older age and usually have comorbidities that limit their ability to collaborate during the examination. Additionally, there were no patients with confirmed RAD, so the efficacy of UltraFast™ ultrasound in this regard was not directly assessed. Further studies in a larger number of patients are required to assess the capacity of UltraFast™ ultrasound in this aspect. To our knowledge, at the time of the writing of this article there are no other peer-review articles on the role of UltraFast™ ultrasound in the assessment of RAD.

Conclusions

In conclusion, this study provides evidence that UltraFast™ ultrasound is faster than conventional Doppler ultrasonography for the assessment of RAD in healthy adults without a history of renal disease. The findings have important implications for clinical practice, as they may suggest that UltraFast™ ultrasound could offer a more efficient and time-saving approach to vascular imaging in patients with suspected RAD. Further research is needed to determine the potential clinical benefits of UltraFast™ ultrasound in different pa-

tient populations and clinical settings. Overall, our results suggest that UltraFast™ is a promising ultrasound technique that warrants further investigation and development.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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Author contributions

Original concept of study: GI, AB. Writing of manuscript: GI, AB, ABJ, FV. Analysis and interpretation of data: GI, AB, ABJ, FV, ML, ED. Final acceptance of manuscript: GI, AB, ABJ, FV, ML, MB, KI, BB, ED. Collection, recording and/or compilation of data: GI, AB, ABJ, FV, MB, KI. Critical review of manuscript: GI, AB, BB, ED.